IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AFFYMETRIX, INC., a Delaware corporation, Plaintiff/Counter-Defendant, v. **ILLUMINA, INC.**, a Delaware corporation, Defendant/Counter-Plaintiff.	Civil Action No.: 04-901 JJF **PUBLIC VERSION**

EXHIBITS TO ILLUMINA'S COUNTER-STATEMENT OF CONTESTED FACTS IN OPPOSITION TO AFFYMETRIX'S MOTION FOR SUMMARY JUDGMENT OF ILLUMINA'S COUNTERCLAIM OF INTENTIONAL INTERFERENCE WITH ACTUAL AND PROSPECTIVE ECONOMIC ADVANTAGE AND PORTIONS OF ILLUMINA'S COUNTERCLAIM FOR UNFAIR BUSINESS PRACTICES

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Original Date: July 28, 2006
Redacted Version: August 18, 2006

EXHIBIT LIST

Exhibit No.	Document
1.	2005 Affymetrix 10K
2.	10/2003 Affymetrix 8K
3.	2002 Affymetrix 10K
4.	Excerpts from Yap deposition
5.	PX560
6.	DX85
7.	Excerpts from Mertzp deposition
8.	Excerpts from Flatley deposition
9.	DX302
10.	Biopoly Money Article
11.	Excerpts from Siegel deposition
12.	Excerpts from Mancilla deposition
13.	DX 82
14.	Excerpts from Lane deposition
15.	Illumina Catalog List 2005
16.	AVI65550-53
17.	AVI55313-14
18.	AVI57962-63
19.	Excerpts from Dance deposition
20.	AVI58733-36
21.	2005 Illumina 10K
22.	AVI62796-97
23.	AVI58376-80

24.	DX456
25.	DX101
26.	AVI84586-96
27.	AVI82349
28.	AVI92039, 59209, 62925, 59210, 80431-39, 59423-38, 81824-25, 62650, 58495-96, 59830-32, 57995-97, 80476-77
29.	AVI62268-73
30.	AVI55929-30
31.	AV56898-99
32.	AVI82089-100
33.	DX100
34.	AVI65002
35.	AVI55289-90
36.	DX434
37.	DX305
38.	AVI84571
39.	Excerpts from Orpin 30(b)(6) deposition
40.	IAFP602431-32
41.	IAFP640191
42.	Excerpts from Orpin deposition
43.	AVI55704-06
44.	AVI58680-83
45.	IAFP640175-76
46.	January 5, 2006 Affymetrix Guidance Announcement
47.	Excerpts from Raimond deposition

48.	AVI63653-54
49.	AVI57846-48
50.	DX206
51.	June 28, 2005 Illumina press release
52.	March 7, 2006 Piper Jaffray Report
53.	Excerpts from Fodor deposition
54.	DX102
55.	AVI57995-97
56.	October 24, 2005 Illumina press release
57.	DX465
58.	DX290
59.	DX103
60.	Gene Logic Supply Agreement
61.	Mertz Deposition Exhibit No. 61
62.	AVI016392
63.	DX71
64.	Excerpts from Lipshutz deposition
65.	Patent License Agreement
66.	AVI056451-53
67.	AVI065133-37
68.	IAFP00535717-719
69.	IAFP00535231
70.	IAFP00570148
71.	DX331
72.	DX284

EXHIBIT 1

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2005

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 (NO FEE REQUIRED)

FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NUMBER 0-28218

AFFYMETRIX, INC.
(Exact name of registrant as specified in its charter)

DELAWARE (State or other jurisdiction of incorporation or organization)	**77-0319159** (IRS Employer Identification Number)
3420 CENTRAL EXPRESSWAY SANTA CLARA, CALIFORNIA (Address of principal executive offices)	**95051** (Zip Code)

(408) 731-5000
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:
None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $0.01
Preferred Stock Purchase Rights

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark if the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b(2) of the Exchange Act. (Check one).

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant at June 30, 2005, based on the closing price of such stock on the Nasdaq National Market on such date, was approximately $1.44 billion. The number of shares of the registrant's Common Stock, $0.01 par value, outstanding on March 2, 2006, was 67,398,440.

DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the Proxy Statement to be filed in connection with the 2006 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K where indicated.

PART I

ITEM 1. BUSINESS

Forward-Looking Statements

All statements in this Annual Report on Form 10-K that are not historical are "forward-looking statements" within the meaning of the federal securities laws, including statements regarding our "expectations," "beliefs," "hopes," "intentions," "strategies" or the like. Such statements are based on our current expectations and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. We caution investors that there can be no assurance that actual results or business conditions will not differ materially from those projected or suggested in such forward-looking statements as a result of various factors, including, but not limited to, the risk factors discussed in "Risk Factors" contained in Item 1A of this report and elsewhere in this report. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

Narrative Description of Business

Overview

We are engaged in the development, manufacture, sale and service of consumables and systems for genetic analysis in the life sciences and clinical healthcare and are recognized as a market leader in creating breakthrough tools that are advancing our understanding of the molecular basis of life. The markets for our products currently include all aspects of molecular biology research in the life sciences, including basic human disease research, genetic analysis, pharmaceutical drug discovery and development, pharmacogenomics (research relating to how a person's genes affect the body's response to drug treatments), toxicogenomics (research relating to the measurement of gene expression as a predictor of toxicity) and molecular diagnostics. Additional markets are emerging in agricultural research, plant breeding, food testing, pathogen identification and consumer genetics. Our integrated GeneChip® microarray platform includes: disposable DNA probe arrays (chips) consisting of nucleic acid sequences set out in an ordered, high density pattern, certain reagents for use with the probe arrays, a scanner and other instruments used to process the probe arrays, and software to analyze and manage genomic or genetic information obtained from the probe arrays. Related microarray technology also offered by us includes licenses for fabricating, scanning, collecting and analyzing results from complementary technologies.

Our business strategy is to capitalize on our leadership position in the DNA microarray field by marketing our GeneChip® technologies to customers based on two central applications: gene expression monitoring and DNA variation detection. Due to the novel, massively parallel approach to studying biological systems that GeneChip® technology enables, numerous discoveries across many disciplines have already been made, as evidenced by the over 4,000 peer-reviewed publications released that have cited GeneChip® technology. The molecular diagnostic application of GeneChip® technologies for diagnosing and guiding treatment of disease is an emerging market opportunity in health management that seeks to improve the effectiveness of health care by collecting information about DNA variation and RNA expression in patients at various times from screening and diagnosis through prognosis and throughout therapeutic monitoring. We currently sell our products directly to pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies as well as academic research centers, government research laboratories, private foundation laboratories and clinical reference laboratories in North America and Europe. We also sell our products through life science supply specialists acting as authorized distributors in Latin America, India, the Middle East and Asia Pacific regions, including China.

In March 1992, Affymetrix, Inc. was incorporated in California as a wholly-owned subsidiary of Affymax N.V. (Affymax) and we have continued our business and operations as Affymetrix. We completed our initial public offering in June 1996 and in September 1998 we reincorporated as a Delaware corporation. Our headquarters and principal research and development facilities are located in Santa Clara, California, and we maintain facilities in West Sacramento, California (probe array manufacturing), Sunnyvale, California (sales, marketing, administration, and array research and development), Emeryville, California (bioinformatics and software development), South San Francisco, California (manufacturing and research and development), Bedford, Massachusetts (instrument development and manufacturing), and additional sales offices in the United Kingdom, Singapore and Japan.

Acquisition

On October 21, 2005, Affymetrix acquired 100% of the outstanding shares of ParAllele BioScience, Inc. ("ParAllele"), a provider of comprehensive genetic discovery solutions to the life science research, pharmaceutical and diagnostic sectors. ParAllele's products and services utilize a unique approach that leverages novel biochemical processes rather than complex instrumentation to discover and analyze minute variations in the human genome. Affymetrix expects the acquisition to accelerate the development and commercialization of new products and create greater opportunities for market penetration and revenue generation as well as increase Affymetrix' core assay development capabilities.

Scientific Background and Technology

Introduction to the Genome and its Opportunity

The genetic content of an organism is known as its "genome." All known genomes are composed of either deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). The instructions required for every living cell to develop its characteristic form and function are believed to be represented within discrete regions of the DNA or RNA known as genes. The instructions contained within genes are embodied in the specific sequences of the four nucleotide bases—adenine–A, cytosine–C, guanine–G and thymine–T (uracil–U replaces T in RNA)—that are the chemical building blocks of DNA and RNA. In protein coding genes, the sequence of these building blocks forms a code which instructs the cell to build a protein, comprised of a string of amino acids, ordered in a way which matches the sequence code of the gene. These proteins are an example of a "hard copy" output of the genetic code and contribute to the structure, biochemical functions and communication mechanisms of the cell in which they are formed.

The DNA molecule possesses a chemical structure which consists of a combination of two DNA strands with hydrogen bonds between nucleotide bases on one strand to complementary nucleotide bases on the other strand. Only certain pairs of the bases can form these complementary bonds: C pairs with G, and A pairs with T. Therefore, a single DNA strand containing bases in the sequence CGTACGGAT can form a bond with a DNA strand containing bases in the sequence GCATGCCTA. Such paired DNA strands are said to be "complementary" and can form a double helix structure in a process called "hybridization." Our GeneChip® technology uses the principle of hybridization to recognize the presence of specific gene sequences and to analyze genetic information.

Genes are segments of DNA that serve as information packets of the genome. In general, a gene's functional information is made available to a cell through the process of transcription or "gene expression," whereby the sequence is copied into an RNA molecule. Protein coding genes may span thousands to hundreds of thousands, or even millions, of nucleotide bases since the non-coding regions of a gene (called "introns") and the coding regions of a gene (called "exons") are usually distributed within neighboring genomic sequences that are not translated into proteins or used, or to the extent currently understood, as a functional part of the gene. The number of distinct protein coding genes in the human genome is estimated to be between 25,000 to 30,000. The number of functional non-coding sequences is the focus of current research interest. Though currently unknown, the number of functional non-coding

Products

Overview

Our products form an integral part of our GeneChip® system that is designed for use by pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies, as well as academic research centers, private government research foundations and clinical reference laboratories. The GeneChip® system consists of several integrated components: disposable probe arrays containing genetic information on a chip, reagents for extracting, amplifying and labeling target nucleic acids, a fluidics station for introducing the test sample to the probe arrays, a hybridization oven for optimizing the binding of samples to the probe arrays, a scanner to read the fluorescent image from the probe arrays, and software to analyze and manage the resulting genetic information. The function of each single-stranded sequence on the GeneChip® probe array is to bind to its complementary single strand of DNA or RNA from a biological sample. Each unique sequence feature on the GeneChip® probe array contains multiple copies of the same single strand of DNA. The nucleic acid (DNA or RNA) to be tested is isolated from a sample, such as blood or biopsy tissue, amplified and fluorescently labeled by one of several standard biochemical methods. The test sample is then washed over the probe array, where the now labeled individual nucleic acid sequences that represent the genetic content or expressed genes of the sample hybridize to their complementary sequences bound on the array. When scanned by a laser, which is part of the scanner instrument, the test sample generates a fluorescent signal. The locations where a fluorescent signal is detected by an optical detection system on the scanner instrument correspond to sequences complementary to the test sample. Sequence variation, or the quantification of specific sequences of nucleic acids in the sample, can be determined by detecting the relative strength of these signals since the sequence and position of each complementary DNA probe on the probe array is known. The combination of a particular GeneChip® probe array, together with an optimized set of reagents and a user protocol describing how to carry out the procedure, is referred to as an "assay."

We currently market products for two principal applications: monitoring of gene expression levels and investigation of genetic variation (DNA analysis including single nucleotide polymorphism (SNP) genotype analysis and resequencing). Our GeneChip® expression monitoring arrays enable our customers to qualitatively and quantitatively measure gene expression levels in a number of biologically relevant organisms. Our catalog GeneChip® expression arrays are available for the study of human, rat, mouse and a broad range of other mammalian and model organisms. Additionally, we market CustomExpress™, CustomSeq™ and NimbleExpress™ products which enable our customers to design their own custom GeneChip® expression arrays or sequence arrays for organisms of interest to them. Our GeneChip® DNA analysis arrays and variant detection systems are available to enable researchers to perform high throughput polymorphism analysis and to carry out large scale resequencing (comparing the DNA sequence of multiple samples against a known reference sequence, e.g. the published human genome sequence). With its unique, parallel analysis capability, GeneChip® technology enables our customers to perform accurate and cost-effective genetic analysis, using minute amounts of sample DNA, in their own laboratories on a scale that was previously only possible in specialist high throughput centers.

In addition, we believe that genetic analysis and testing products will be a core component in the area of clinical research and molecular diagnostic applications and we are developing our GeneChip® system for clinical research and diagnostic analysis of both gene expression and DNA analysis. Together with our collaborative partners, we are focusing on the development and commercialization of diagnostic products in cancer, osteoporosis, cardiovascular, inflammatory, metabolic, infectious and other diseases, and believe that our GeneChip® assays will facilitate more efficient and effective disease detection, prognosis and treatment selection, leading to overall improved patient management. To further our clinical research and molecular diagnostics strategy, we have established partnerships and customer relationships with leading academic researchers, pharmaceutical and biotechnology companies, including F. Hoffmann-La Roche Ltd. ("Roche"), bioMérieux, Inc. ("bioMérieux"), and Veridex, LLC, a Johnson & Johnson

company ("Veridex"). We believe that the rapid growth of the clinical research and the diagnostic devices markets holds the potential for GeneChip® technology applications ranging from basic research to clinical trials and, ultimately, diagnostic devices. As a result we are working with leaders in molecular diagnostics to provide custom made GeneChip® probe arrays to their specifications. Our partners subsequently package the chips into kits, seek regulatory approval for their diagnostic use, and sell them into the diagnostic markets using their sales channels. We are leveraging our partners' strengths in research, development, regulatory practices and distribution while leveraging our strengths in array technology. These products are marketed as being Powered by Affymetrix™.

Gene Expression Monitoring Arrays

Gene expression monitoring is a valuable tool for identifying correlations between genes, determining their biological functions and identifying patterns that might be useful in classifying diseases. To monitor gene expression, we design and manufacture probe arrays with single-stranded DNA molecules that are complementary to sequences within genes of interest. By synthesizing specific probes for multiple genes on a single probe array, we enable researchers to quickly, quantitatively and simultaneously monitor the expression of a large number of genes of interest. By monitoring the expression of such genes under different conditions and at different times, researchers can use the probe arrays to understand the dynamic relationship between gene expression and biological activity. We believe such information will be an important tool in understanding gene function and for the development of new drugs and diagnostic tools. Increasingly, clinical research is showing that gene expression patterns in tissue samples, particularly those from cancerous tissues, can be used to characterize disease sub-types and hopefully to predict therapeutic responses and likely outcomes.

The range of GeneChip® Expression products is described below:

- *Standard Expression Monitoring Arrays.* We are currently selling a portfolio of standard expression monitoring GeneChip® arrays. Our current offering of standard arrays includes products that monitor the expression of the majority of full-length and partial gene sequences contained in publicly available sequence databases, which correspond with human, mouse, rat, canine, Drosophila melanogaster (fruit fly), Caenorhabditis elegans (nematode), Xenopus laevis (frog), Danio rario (zebrafish), Saccharomyces cerevisiae (yeast), Escherichia coli (bacteria), Pseudomonas aeruginosa (bacteria), Plasmodium falciparum (malarial parasite), Anopheles (mosquito vector of malaria), Arabidopsis thaliana (mustard plant, a common model organism for plants), bovine (cow), chicken, maize (corn), medicago (alfalfa), poplar (tree), porcine (pig), Rhesus macaque (monkey), rice, soy, sugar cane, tomato, Vitis vinifera (wine grapes) and citrus arrays.
- *GeneChip® Exon Arrays.* We are now offering exon arrays that interrogate the expression of individual exons, the building blocks that make up a transcript. It is well known that alternative utilization of different exons from the same gene (known as alternative splicing) leads to the generation of various protein products, leading to diverse functional consequences. In addition, mis-regulation of splicing has been associated with many different diseases including cancer and diabetes. The exon array is the first experimental tool to discover new splicing events on a genome-wide scale to help researchers better understand disease mechanisms which can lead to the design of novel therapies for treatment and more informative diagnostic signatures.
- *Whole Genome Tiling Arrays.* We offer tiling arrays for the genomes of a number of major organisms including human, mouse, drosophila, C.elegans and yeast. These designs use evenly spaced probes across the non-repetitive portion of the genome and rely only on genomic DNA sequence and not functional annotation for their design. The arrays are used for mapping the entire collection of transcribed elements (including non-coding RNAs that are used for structural and regulatory purposes), identifying protein binding and methylation sites and identification of genomic origins of replication.

- *Custom Express Arrays.* We have established a GeneChip® CustomExpress™ Array Program enabling customers to design affordable arrays tailored to their specific research needs. Our CustomExpress™ arrays enable customers to select probes from any of our probe sequences on our catalog arrays and/or to incorporate probes from their own proprietary gene sequences. These arrays are then produced utilizing the same manufacturing technologies as our other GeneChip® whole genome expression arrays.
- *Made-to-Order Arrays.* We offer the GeneChip® Made-to-Order Array Program to enable our customers to use arrays from selected custom designs and previous-generation GeneChip® arrays which are no longer available as catalog products.

DNA Analysis Arrays

As genes and regulatory regions in the human genome are mapped, identified, and sequenced, the value of understanding the variability of sequences among individuals increases. Researchers seek to determine the normal sequence of the gene, which mutations or polymorphisms exist in a population, and whether these variations correlate with a disease or other aspect of the human condition. Studies of the genetics of complex diseases have historically been challenging due to high costs of sequencing or genotyping of large numbers of affected and unaffected individuals. Genetic variation also impacts how individuals respond to therapeutics. The study of these effects is known as pharmacogenetics. This is part of the broader field of pharmacogenomics, which seeks to understand how the overall composition and expression of the genome affects therapeutic response, drug efficacy and the incidence of adverse side effects to therapy. We believe pharmacogenomics will become increasingly important both in clinical drug trials and patient care. By using our resequencing and genotyping technologies, we believe that our GeneChip® probe arrays could significantly reduce the cost and time required for high-volume polymorphism analysis, which is currently performed through more labor-intensive techniques.

We have initiated product research and development efforts on several genetic analysis probe arrays and variant detection analysis systems and formed collaborations to accelerate the development of our genotyping products. For additional information concerning these efforts and collaborations see the sections of this Form 10-K entitled "Research and Development" and "Our Collaborative Partners." We currently market the following DNA analysis products:

- *GeneChip® Human Mapping 500K Set.* The Mapping 500K Set is our newest whole genome genotyping product and the third in a family of products for large scale genome-wide genotyping using a simple, scalable, one-primer assay. The 500K Set genotypes over 500,000 SNPs on a two array set. The 500K Set is enabling novel genetic experiments (called genome-wide association studies) to understand the genes involved in complex disease and drug response using real-world disease populations. Researchers have for many years sought to study major diseases in unrelated populations, but the information density (hundreds of thousands of markers) and experiment size (hundreds or thousands of samples) made these experiments unaffordable. The 500K Set is the first and market leading product in making large scale whole genome analysis cost effective.
- *GeneChip® Human Mapping 100K Set and 10K Array.* We offer two other products based on the same scalable one primer assay as our 500K product: the 100K Set and the 10K Array. The 100K Set genotypes over 100,000 SNPs on a two array set and the 10K Array genotypes over 10,000 SNPs on a single array. The 100K Set was the first product to enable genome-wide association studies and is also used for chromosomal copy number analysis. The 10K Array is used primarily for linkage analysis, the study of the inheritance of disease in families.
- *Targeted Genotyping Products.* We offer a variety of targeted genotyping products for the analysis of between 1,500 and 20,000 SNPs per sample, using a highly multiplexed assay for use with GeneChip® Universal Tag Arrays. This innovative assay enables customers to genotype selected

SNPs in a single assay with only one primer per SNP. We offer the widest variety of standard panels of pre-selected SNPs for major diseases (e.g., inflammatory disease), model organisms (e.g., mouse), and specific applications (e.g., drug metabolizing enzymes), as well as custom capabilities that offer customers the highest conversion rates to genotype more of the SNPs they want.

The assay described above and the products offered through this product line represent the technology and products acquired through the ParAllele acquisition described elsewhere in this report.

- *GeneChip® CustomSeq™ Resequencing Arrays.* Version 2 of this product line was released in 2005, increasing sequence content per array by tenfold. The CustomSeq™ sequence variation product line now enables customers to sequence up to 300,000 bases on one array in just two days with high accuracy. CustomSeq™ arrays offer researchers a powerful complementary tool to our whole genome genotyping and whole genome expression products on the same industry-standard GeneChip® platform, and are currently being used in a wide variety of applications ranging from infectious disease research to detailed sequence analysis following up association studies to full mitochondrial genome sequencing.

DNA Analysis Products Powered by Affymetrix™

- *Roche AmpliChip™ CYP450.* The Powered by Affymetrix™ program and collaboration with Roche announced in January 2003 resulted in the June 2003 release of the Roche AmpliChip™ CYP450 microarray. The AmpliChip CYP450 microarray allows for complex sequence information to be analyzed for the purpose of genotyping the CYP2D6 and CYP2C19 genes. Sequence variation in these genes can result in marked differences in the way individuals metabolize, and hence respond to, an estimated 25% of all drugs. In late 2004, Roche obtained in-vitro diagnostic status for the product in the United States and Europe.

Access Programs for Our GeneChip® Arrays

We offer a variety of sales programs for our gene expression monitoring and DNA analysis arrays, tailored to the needs of industrial, biotech and academic/government customers. These programs are tied to volume usage and customers can select a program that best meets their needs to receive favorable pricing per array.

Reagents for Our GeneChip® Systems

Our GeneChip® reagent kits contain validated reagents critical for the success of expression monitoring and DNA analysis experiments. The 2005 additions to the Affymetrix GeneChip® reagent family are listed below:

Whole Transcript Reagents. With the launch of the GeneChip® Whole Transcript (WT) Sense Target Labeling Assay, we introduced: GeneChip® WT Terminal Labeling Kit and GeneChip® WT cDNA Synthesis and Amplification Kit, each available in 10 or 30 reactions.

Array Station Reagents. We introduced two new GeneChip® reagent kits developed and optimized specifically for target preparation on the GeneChip® Array Station: GeneChip® HT One-Cycle cDNA synthesis Kit and GeneChip® HT IVT Labeling Kit in 96 reactions.

Mapping 500K Reagents. With the launch of the GeneChip® Human Mapping 500K Array Set, we introduced the GeneChip® Mapping 250K Sty Assay Kit and the GeneChip® Mapping 250K Nsp Assay Kit, each available in 30 or 100 reactions.

Hybridization Wash and Stain Reagents. In December 2005 we introduced the GeneChip® Hybridization Wash and Stain Kit which contains reagents formulated into the fewest number of individual components possible.

For our expression probe arrays, we offer the following reagents: One-Cycle cDNA Synthesis Kit, Two-Cycle cDNA Synthesis Kit, GeneChip® Expression 3'-Amplification Reagents for IVT Labeling, GeneChip® Sample Cleanup Module, GeneChip® IVT cRNA Clean up Kit, T7-Oligo(dT) Promoter Primer Kit, Eukaryotic Poly-A RNA Control Kit and Eukaryotic Hybridization Control Kit, GeneChip® WT Terminal Labeling Kit, GeneChip® WT cDNA Synthesis and Amplification Kit, GeneChip® HT One-Cycle cDNA synthesis Kit, GeneChip® HT IVT Labeling Kit, and the GeneChip® Hybridization Wash and Stain Kit.

For our DNA analysis arrays, we offer the following reagents: GeneChip® Resequencing Assay Kit, GeneChip® Mapping 10K Xba Assay Kit, GeneChip® Mapping 50K Xba Assay Kit, GeneChip® Mapping 50K Hind Assay Kit, GeneChip® Mapping 250K Sty Assay Kit and the GeneChip® Mapping 250K Nsp Assay Kit.

Instruments for Our GeneChip® Systems

Our GeneChip® instruments provide a fully integrated system for conducting research using GeneChip® probe arrays. The instrument system consists of four hardware devices, each providing for robust preparation and analysis of samples using GeneChip® arrays. The first device is a hybridization oven to control the timing and temperature required for hybridization of the test sample to the probe array. The second device is a fluidics station that controls exposure of the probe array to solutions containing prepared sample and labeled detection reagents across the probe array. The fluidics station can process four probe arrays simultaneously. The fluidics station protocols conclude with a reagent wash that leaves the labeled, hybridized test sample bound to the probe array.

The third device, a laser scanner, is used after completion of protocols on the fluidics and hybridization stations, at which time the cartridge containing the probe array is placed in the scanner and read. The scanner consists of a laser, high-resolution optics, robotics to position and scan the probe array, a fluorescence detector and an interface to a computer workstation. The labeled material that is bound to the hybridized test sample emits fluorescent signals when exposed to the light from the laser. The locations and intensities of the fluorescent signals are recorded by the scanner and stored in the computer for analysis. The fourth device is an autoloader, which is a 48-array carousel that interfaces with the scanner to allow walk-away automation of the scanning steps, while maintaining the loaded arrays at the optimum storage temperature.

The individual components of our GeneChip® instrument system are described in more detail below.

- *GeneChip® Hybridization Oven 640.* The GeneChip® Hybridization Oven 640 is used to control the timing and temperature required for hybridization of the test sample to the probe array. The GeneChip® Hybridization Oven 640 holds up to eight probe array cartridge carriers (each with eight cartridge slots) that rotate for controlled hybridization of up to 64 probe arrays. This unit delivers temperature control for consistent performance across all probe array applications.
- *Fluidics Station 450.* The Fluidics Station 450 is used to control exposure of the probe array to solutions containing prepared sample and labeled detection reagents across the probe array and can independently process four probe arrays simultaneously. The fluidics station protocols conclude with a reagent wash that leaves the labeled, hybridized test sample bound to the probe array. Multiple fluidics stations can be connected to the same computer workstation in order to expedite array processing in high throughput laboratories.

- *GeneChip® Scanner 3000.* The GeneChip® Scanner 3000 uses proprietary laser scanning technology and high resolution optics to read the fluorescent signal from GeneChip® arrays. The GeneChip® Scanner 3000, developed and manufactured by Affymetrix, represents the next generation in scanner technology. The Flying Objective™ scanning technology incorporated into this scanner has been adapted to provide faster scanning of GeneChip® probe arrays with a high degree of image uniformity and accuracy. The current version of the GeneChip® Scanner 3000 has been validated to allow imaging of GeneChip® arrays with feature sizes as small as 5 microns and can support multicolor assays. The GeneChip® Scanner 3000 is purchased with a computer workstation loaded with Affymetrix GeneChip® Operating Software ("GCOS") (discussed below under "Software for Our GeneChip® Systems and Analysis Tools").
- *GeneChip® AutoLoader.* The GeneChip® AutoLoader, developed and manufactured by Affymetrix, is a 48–array carousel that automatically loads and unloads arrays from the scanner, helping researchers automate their array processing and providing walk–away use in the lab. The GeneChip® Scanner with AutoLoader can load and scan 48 current catalog arrays in 28 hours or less, depending on the feature size and array format that is scanned. Thermostatic control allows the stored arrays to be held in a cooled environment and then warmed to optimum temperature for scanning. The AutoLoader attaches to the top of the scanner, saving valuable bench space, and does not require any additional power source.
- *Workstations.* We offer workstations to accommodate varied research needs. The Type I GeneChip® Workstation (Windows NT) is configured with system software enabling it to operate the GeneChip® Scanner 3000 and multiple Fluidics Stations. Our Type II GeneChip® Workstation (Windows NT and Windows 2000) can operate independently of the scanner and fluidics station instruments.
- *GeneChip® Array Station.* Through our collaboration with Caliper Life Sciences, Inc., we launched the Affymetrix GeneChip® Array Station that has the capacity to process hundreds of biological samples per week with minimal human supervision, reducing operating costs and variability in target preparation in 2005. The GeneChip® Array Station is designed to perform target preparation for both cartridges and array plates as well as perform the wash and stain function for the array plates. The GeneChip® Array Station adapts the same industry–standard GeneChip® technology to a standard 96–well microtiter plate, and runs on an automated system built with off–the–shelf robotic components. In addition, we launched the GeneChip® HT Scanner that utilizes CCD based technology for imaging of the new array plates. The GeneChip® Array Station automates the most labor intensive steps in GeneChip® probe array processing, dramatically reducing the cost per assay. The decrease in cost and increase in throughput makes the GeneChip® Array Station well suited for downstream development applications such as compound profiling, molecular toxicology and clinical trials.

Software for Our GeneChip® Systems and Analysis Tools

Our "GCOS" software is supplied as part of an integrated system and runs on an industry standard PC platform. The fluorescence intensity data captured from the scanner are used in conjunction with computer files containing the probe sequence and location of all the probes on the probe array to determine the expression level of a particular gene or to identify particular DNA sequence variations of the test sample.

Our Data Mining Tool® and GeneChip® Operating Software Server ("GCOS Server") software products allow for sophisticated analyses of gene expression results and provide a means of linking and integrating this information with other databases.

Customers may choose operating or other software products provided by third party vendors that have been developed through our OpenSystems™ program, which includes the provision of a Software Developer's Kit to interested commercial and academic parties. Through this program we intend to stimulate a wide range of independent groups to develop tools for use with our platform, further enhancing our customers' capability to generate unique biological insights from the high quality data provided by the GeneChip® platform.

Finally, our NetAffx™ Analysis Center (www.affymetrix.com/analysis/) is our exclusive online informatics resource for our customers and provides streamlined, open access to design information and biological annotations associated with our GeneChip® arrays. It was created to assist genomic researchers with the design and analysis of DNA array based experiments. NetAffx™ offers researchers a searchable catalog of Affymetrix GeneChip® probe array content, a range of publicly available and Affymetrix generated databases, and links to important third party resources.

Instruments for Use in Molecular Diagnostics

The GeneChip® System 3000Dx (GCS3000Dx) is configured especially for the molecular diagnostic market. In September 2004, the GCS3000Dx received Conformite Europeene (CE) certification, clearing it for use as an in–vitro diagnostic (IVD) product in the European Union. In December 2004, the GCS3000Dx was also cleared by the United States Food and Drug Administration (FDA) as an IVD to be used in conjunction with the Roche Diagnostics AmpliChip™ CYP450 Test. The AmpliChip™ CYP450 Test also received CE certification and FDA clearance in 2004 making it the first Powered by Affymetrix™ IVD test. This test, which utilizes an Affymetrix microarray produced specifically for Roche Diagnostics, analyzes a patient's Cytochrome P450 2D6 and 2C19 genotypes to look for variations that can influence drug metabolism. The GCS3000Dx will support all Powered by Affymetrix™ molecular diagnostic tests. The system includes the GCS3000Dx Scanner with Autoloader Dx, FS450Dx Fluidics Station, and Workstation with GCOS Dx software.

We believe that our GeneChip® technology can be effectively applied to complex molecular diagnostic testing. We have formed collaborations and intend to further partner with, or license technology to, established diagnostic and medical device companies to develop, obtain regulatory approval for, and commercialize probe arrays and instrumentation. We anticipate broader use of probe arrays as components of diagnostic products and clinical research applications. We believe that to support large central laboratories, additional instrumentation and automation will need to be developed to allow for handling the large volume testing of the clinical diagnostic setting. To further our molecular diagnostics strategy, we have established a number of collaborations with leading academic researchers, diagnostic companies, pharmaceutical and biotechnology companies.

For example, we are non–exclusively collaborating with Roche to develop and commercialize GeneChip® diagnostic tests for DNA analysis, genotyping and resequencing applications, as well as for RNA expression analysis, in a broad range of human disease areas. Using our GeneChip®technologies, Roche intends to develop and market diagnostic tests for diseases such as cancer and osteoporosis and cardiovascular, metabolic, infectious and inflammatory diseases.

In oncology, we are non–exclusively collaborating with Veridex, a Johnson & Johnson company, to develop and commercialize GeneChip® diagnostic tests for oncology. Using our GeneChip® technologies, Veridex intends to develop and market tests for cancer.

We have a non–exclusive collaborative development agreement and an associated supply agreement for probe arrays with bioMérieux, Inc. in breast cancer and in bacteriology to identify the species and drug resistance profiles of those bacteria causing human infection. The agreements also allow for non–exclusive development of DNA probe arrays for certain diagnostic viral tests and for the fields of food and industrial testing.

In the United States, third-party payor price resistance, the trend towards managed health care and legislative proposals to reform health care or reduce government insurance programs could reduce prices for health care products and services, adversely affect the profits of our customers and collaborative partners and reduce our future royalties and product sales.

Environmental Matters

We are dedicated to compliance and protection of the environment and individuals. Our operations require the use of hazardous materials (including biological materials) which subject us to a variety of federal, state and local environmental and safety laws and regulations. We believe we are in material compliance with current and applicable laws and regulations. However, some of the regulations under the current regulatory structure allow for "strict liability," holding a party potentially liable without regard to fault or negligence. We could be held liable for damages and fines as a result of our, or others', business operations should contamination of the environment or individual exposure to hazardous substances occur. We cannot predict how changes in these laws or development of new regulations will affect our business operations or the cost of compliance.

Employees

As of March 2, 2006, we had 1,101 full-time employees. The employee group includes chemists, engineers, computer scientists, mathematicians and molecular biologists with experience in the diagnostic products, medical products, semiconductor, computer software and electronics industries. None of our employees are represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that we maintain good relationships with our employees. Our success depends in large part on our ability to attract and retain skilled and experienced employees.

Seasonality

Customer demand for probe arrays and instrumentation systems is typically highest in the fourth quarter of the calendar year as customers spend unused budget allocations before the end of the financial year.

Backlog

Because most customer orders are shipped in the quarter in which they are received, we believe that backlog at quarter end is typically not a material indicator of future sales. In addition, backlog may not result in sales because of cancellation of orders or other factors. On a few occasions we have experienced, and made public announcements about, short-term increases in backlog as a result of factors such as new product introductions or supply constraints. For example, due to low initial production yields on our new Mapping 500K Array product we announced that probe array shipments were constrained during the third and fourth quarters of fiscal 2005. Although these capacity constraints may have increased our backlog with respect to our Mapping 500K Array product, we continue to believe that backlog information is not material to an understanding of our business taken as a whole.

Financial Information About Industry Segments

We operate in one business segment, for the development, manufacture, and commercialization of systems for genetic analysis in the life sciences and diagnostic industry. Our operations are treated as one segment as we only report operating information on a total enterprise level to our chief operating decision-makers. Further, resource allocations are also made at the enterprise level by our chief operating decision-makers.

EXHIBIT 2

Form 8-K

AFFYMETRIX INC - AFFX

Filed: October 22, 2003 (period: October 22, 2003)

Report of unscheduled material events or corporate changes.

Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):
October 22, 2003 (October 22, 2003)

AFFYMETRIX, INC.
(Exact name of registrant as specified in its charter)

DELAWARE	**0-28218**	**77-0319159**
(State of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

3380 Central Expressway, Santa Clara, California 95051
(Address of principal executive offices) (Zip Code)

(408) 731-5000
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Item 7. FINANCIAL STATEMENTS AND EXHIBITS

(c) Exhibits

Exhibit Number	Description
99.1	Press Release issued by Affymetrix, Inc. dated October 22, 2003.

Item 9. REGULATION FD DISCLOSURE (Information Furnished in this Item 9 is Furnished Under Item 12. RESULTS OF OPERATIONS AND FINANCIAL CONDITION)

On October 22, 2003, Affymetrix, Inc. (the "Company") issued a press release announcing the Company's operating results for the quarter ended September 30, 2003. A copy of the Company's press release is attached hereto as Exhibit 99.1.

The information furnished in Items 9 and 12 of this Current Report on Form 8-K, including the exhibit, shall not be deemed to be incorporated by reference into Affymetrix' filings with the SEC under the Securities Act of 1933.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AFFYMETRIX, INC.

By: /s/ Barbara A. Caulfield
Name: Barbara A. Caulfield
Title: Executive Vice President and General Counsel

Date: October 22, 2003

EXHIBIT INDEX

Exhibit Number	Description
99.1	Press Release issued by Affymetrix, Inc. dated October 22, 2003.

EXHIBIT 99.1

FOR IMMEDIATE RELEASE

Investor Contact:
Doug Farrell
Vice President of Investor Relations
408-731-5285

Media Contact:
Anne Bowdidge
Director, Global Public Relations
408-731-5925

AFFYMETRIX REPORTS RECORD PRODUCT REVENUE AND PROFIT

- Next Generation GeneChip® Technology Drives Revenue Growth -

Santa Clara, Calif. — October 22, 2003 — Affymetrix, Inc., (Nasdaq: AFFX) today reported its operating results for the third quarter ended September 30, 2003. The Company reported net income of approximately $5.8 million or $0.10 per basic and diluted share in the third quarter of 2003, as compared to net income of $0.6 million or $0.01 per basic and diluted share in the third quarter of 2002.

Total revenue for the quarter was $76.2 million, of which $2.7 million was related to the sale of products and wafers to Perlegen Sciences, Inc., compared to total revenue of $72.8 million in the third quarter of 2002, of which $4.9 million was related to the sale of products and wafers to Perlegen.

Product and product related revenue increased to $71.1 million for the third quarter of 2003, compared to $62.9 million in the same period in 2002. Third quarter product sales included GeneChip® array revenue of $34.3 million and record instrument revenue of $18.1 million. The combination of next generation system purchases and upgrades contributed to strong instrument sales for the quarter.

Royalties and other revenue were $2.3 million for the third quarter of 2003 compared to $5.0 million in the third quarter of 2002.

Total costs and expenses for the quarter were $68.8 million compared to $71.0 million in the third quarter of 2002.

Cost of product and product related revenue was $24.7 million in the third quarter of 2003 compared to $22.2 million in the same period of 2002. Product and product related gross margin was 65.3% in the third quarter compared to 64.7% in the third quarter of 2002.

Research and development expenses were $16.5 million during the third quarter of 2003 compared to $16.7 million in the third quarter of 2002.

Selling, general and administrative expenses were $24.1 million for the third quarter of 2003 compared to $24.9 million in the third quarter of 2002.

Quarterly Highlights

- Affymetrix began commercialization of 11-micron technology, expanding our CustomExpress offering to include arrays containing over 1.3 million probes. This format provides more information while saving customers time and money.
- Affymetrix launched the world's first catalog human genome on a single array, the GeneChip brand Human Genome U133 Plus 2.0 Array, making whole-genome research even more accessible to individual researchers.
- The Company posted record instrument revenue as new customers purchased systems and the current installed base continued to upgrade to next generation GeneChip technology.
- Affymetrix began shipping the new GeneChip brand AutoLoader for the GeneChip Scanner 3000, helping researchers automate their array processing.
- The Company introduced the first automated HighThroughputArray (HTA™) GeneChip platform, with Johnson & Johnson Pharmaceutical Research & Development as our first partner for the HTA system, marking the industrialization of microarray technology. This combination of industry-standard 96-well microtiter-based technology with the gold standard in microarray technology is expected to increase output through automation and drive down the cost per experiment.
- In an industry first, Affymetrix released genotyping data on over 120,000 validated SNPs into the public domain. These SNPs will be offered to researchers worldwide on the upcoming GeneChip 100K SNP product and will be linked to publicly available genome databases.
- In order to further the community's access to gold standard array technology, the Company added Paradigm Genetics to our growing base of authorized service providers.

Financial Outlook

For fiscal 2003, the Company expects product and product related revenue of approximately $280 million and total revenue of approximately $300 million.

Affymetrix' management team will host a conference call to review its operating results for the third quarter and provide financial guidance for the remainder of 2003. A live webcast of the conference call can be accessed by visiting the Investor Relations section of the Company's website at www.affymetrix.com. In addition, investors and other interested parties can listen by dialing domestic: (888) 737-3798, international: (706) 643-2578 on October 22 at 2:00 p.m. PT. A replay of the conference call will be available until 5:00 p.m. PT on October 29 at the following numbers: domestic: (800) 642-1687, international: (706) 645-9291; passcode for both: #2751846. An archived webcast of the conference call will be available under Investor Relations section of the Company's website at www.affymetrix.com.

About Affymetrix

Affymetrix is a pioneer in creating breakthrough tools that are driving the genomic revolution. By applying the principles of semiconductor technology to the life sciences, Affymetrix develops and commercializes systems that enable scientists to improve the quality of life. The Company's customers include pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies as well as academic, government and other non-profit research institutes.

Affymetrix offers an expanding portfolio of integrated products and services, including its integrated GeneChip platform, to address growing markets focused on understanding the relationship between genes and human health. Additional information on Affymetrix can be found at www.affymetrix.com.

All statements in this press release that are not historical are "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act as amended, including statements regarding Affymetrix' "expectations," "beliefs," "hopes," "intentions," "strategies," or the like. Such statements, including Affymetrix' financial outlook for 2003, are subject to risks and uncertainties that could cause actual results to differ materially for Affymetrix from those projected, including, but not limited to, risks of the Company's ability to achieve and sustain higher levels of revenue, higher gross margins, reduced operating expenses, market acceptance, personnel retention, uncertainties relating to the length and severity of the current global economic weakness, the reduction in overall capital spending in the academic and biotechnology sectors, changes in government funding policies, unpredictable fluctuations in quarterly revenues, uncertainties related to cost and pricing of Affymetrix products, dependence on collaborative partners, uncertainties relating to sole source suppliers, uncertainties relating to FDA, and other regulatory approvals, competition, risks relating to intellectual property of others and the uncertainties of patent protection and litigation. These and other risk factors are discussed in Affymetrix' Form 10-K for the year ended December 31, 2002 and other SEC reports, including its Quarterly Reports on Form 10-Q for subsequent quarterly periods. Affymetrix expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Affymetrix' expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

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AFFYMETRIX, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(IN THOUSANDS)
(UNAUDITED)

	September 30, 2003	December 31, 2002 (Note 1)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 50,387	$ 67,888
Available-for-sale securities	279,150	293,570
Accounts receivable, net	55,198	63,986
Inventories	24,042	26,739
Prepaid expenses and other current assets	4,250	3,770
Total current assets	413,027	457,953
Property and equipment, net	63,499	72,836
Acquired technology rights, net	28,362	23,039
Goodwill	18,601	18,601
Notes receivable from employees	1,589	1,674
Other assets	27,979	27,300
Total assets	$ 553,057	$ 601,403
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$ 53,714	$ 66,864
Deferred revenue—current portion	29,713	19,381
Common stock purchase rights	3,000	—
Other current liabilities	6,376	—
Total current liabilities	92,803	86,245
Deferred revenue—long-term portion	46,919	—
Other long-term liabilities	2,983	8,322
Convertible subordinated notes	267,460	368,900
Common stock purchase rights	—	3,000
Stockholders' equity:		
Common stock	591	585
Additional paid-in capital	363,758	355,515
Notes receivable from stockholders	(417)	(720)
Deferred stock compensation	(5,571)	(8,015)
Accumulated other comprehensive (loss) income	(800)	515
Accumulated deficit	(214,669)	(212,944)
Total stockholders' equity	142,892	134,936
Total liabilities and stockholders' equity	$ 553,057	$ 601,403

Note 1: The condensed consolidated balance sheet at December 31, 2002 has been derived from the audited consolidated financial statements at that date included in the Company's Form 10-K for the fiscal year ended December 31, 2002.

AFFYMETRIX, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(IN THOUSANDS, EXCEPT PER SHARE AMOUNTS)
(UNAUDITED)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2003	2002	2003	2002
Revenue:				
Product sales	$ 57,467	$ 50,973	$ 153,441	$ 144,721
Product related revenue	13,625	11,961	41,992	34,069
Total product and product related revenue	71,092	62,934	195,433	178,790
Royalties and other revenue	2,349	4,971	8,194	16,331
Revenue from Perlegen Sciences	2,744	4,868	8,005	16,454
Total revenue	76,185	72,773	211,632	211,575
Costs and expenses:				
Cost of product sales	22,393	20,942	56,210	60,298
Cost of product related revenue	2,304	1,287	6,805	3,657
Cost of revenue from Perlegen Sciences	2,744	4,868	8,005	16,454
Research and development	16,463	16,732	48,990	50,747
Selling, general and administrative	24,092	24,929	76,250	71,414
Amortization of deferred stock compensation	484	1,966	1,852	7,607
Amortization of purchased intangibles	281	282	844	844
Charge for acquired in-process research and development	—	—	10,096	—
Total costs and expenses	68,761	71,006	209,052	211,021
Income from operations	7,424	1,767	2,580	554
Interest income and other, net	2,403	3,982	10,765	10,289
Interest expense	(3,559)	(4,930)	(13,726)	(14,788)
Net income (loss) before income taxes	6,268	819	(381)	(3,945)
Income tax provision	(466)	(200)	(1,344)	(601)
Net income (loss)	$ 5,802	$ 619	$ (1,725)	$ (4,546)
Basic and diluted net income (loss) per share	$ 0.10	$ 0.01	$ (0.03)	$ (0.08)
Shares used in computing basic net income (loss) per share	58,881	58,075	58,717	57,940
Shares used in computing diluted net income (loss) per share	60,485	59,539	58,717	57,940

EXHIBIT 3

QuickLinks -- Click here to rapidly navigate through this document

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2002

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 (NO FEE REQUIRED)**

FOR THE TRANSITION PERIOD FROM_____ TO_____

COMMISSION FILE NUMBER 0-28218

AFFYMETRIX, INC.
(Exact name of registrant as specified in its charter)

DELAWARE (State or other jurisdiction of incorporation or organization)	**77-0319159** (IRS Employer Identification Number)
3380 CENTRAL EXPRESSWAY **SANTA CLARA, CALIFORNIA** (Address of principal executive offices)	**95051** (Zip Code)

(408) 731-5000

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $0.01

Preferred Stock Purchase Rights

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes ☒ No ☐

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant at June 28, 2002, based on the closing price of such stock on the Nasdaq National Market on such date, was approximately $1,194.5 million.

The number of shares of the registrant's Common Stock, $.01 par value, outstanding on March 20, 2003, was 58,788,170.

DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the Proxy Statement to be filed in connection with the 2003 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K Report where indicated.

PART I

ITEM 1. BUSINESS

Item 1. Business

Forward-Looking Statements

All statements in this Annual Report on Form 10-K that are not historical are "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act as amended, including statements regarding our "expectations," "beliefs," "hopes," "intentions," "strategies" or the like. Such statements are based on our current expectations and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. We caution investors that there can be no assurance that actual results or business conditions will not differ materially from those projected or suggested in such forward-looking statements as a result of various factors, including, but not limited to, the risk factors discussed in this Annual Report on Form 10-K on page 26. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

Narrative Description of Business

Overview

We are engaged in the development, manufacture, sale and service of systems for genetic analysis in the life sciences and are recognized as a market leader in creating breakthrough tools that are driving the genomic revolution. Our integrated GeneChip® platform includes disposable DNA probe arrays (chips) consisting of gene sequences set out in an ordered, high density pattern, certain reagents for use with the probe arrays, a scanner and other instruments to process the probe arrays, and software to analyze and manage genomic information from the probe arrays. Related microarray technology offered by us includes instrumentation, software and licenses for fabricating, scanning and collecting and analyzing results from low density microarrays. We commenced our first commercial sale for research use in August 1994, with broader commercial sales beginning in April 1996.

Our business strategy is to capitalize on our leadership position in the DNA probe array field by applying our GeneChip® technologies to three primary areas: gene expression monitoring, DNA analysis and clinical applications. The clinical applications for GeneChip® technologies for diagnosing and treating disease is an emerging market opportunity in health management that seeks to improve the effectiveness of health care by collecting genetic and RNA expression information on patients at various times from prognosis, through diagnosis and on to the end of therapy. The markets for our products include all aspects of molecular biology research in the life sciences, including basic human disease research, genetic analysis, pharmaceutical drug discovery and development, pharmacogenomics (research relating to how a person's genes affect the body's response to drug treatments), toxicogenomics (research relating to the measurement of gene expression as a predictor of toxicity) and agricultural research. We currently sell our products directly to pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies as well as academic research centers, government research laboratories, private foundation laboratories and clinical reference laboratories in North America, Europe and Japan. We also sell our products through life science supply specialists acting as authorized distributors in Europe and the Asia Pacific region.

We commenced our business and operations in 1991 through Affymax N.V. ("Affymax"), a company organized under the laws of the Netherlands. In March 1992, Affymetrix, Inc. was incorporated in California as a wholly-owned subsidiary of Affymax and we have continued our business and operations as Affymetrix. We completed our initial public offering in June 1996 and in

EXHIBIT 4

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 5

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 6

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 7

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 8

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 9

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 10

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Wired News

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Wired News Search

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Issue 8.06 - June 2000

Biopoly Money

Patents and strong-arm tactics are helping make Affymetrix the Intel of biochips. Along the way, Affy wants to turn DNA into a proprietary system.

By Brian Alexander

They've got to be kidding. The entire corporate leadership of Affymetrix - maker of a DNA microarray known as the GeneChip, a device that may help determine whether I will be sexually potent, keep my hair, or bench-press 250 pounds at age 85 - wants to know why the company has attracted so much negative attention for its business tactics over the last several months.

For the past three hours, I've been sitting in a bland Santa Clara, California, conference room inside a generic concrete office block honeycombed with cubicles, listening to CEO Stephen Fodor, president Susan Siegel, executive vice-president Ken Nussbacher, CFO Edward Hurwitz, and general counsel Vern Norviel insist on how badly Affy is misunderstood - that they're just a bunch of good people trying to make a buck the Silicon Valley way, no different from Cisco or Intel. The executives feel put upon by pestering media, competitors, and academic critics who argue that tools like the DNA microarray should, in the name of progress, be made widely and cheaply available to researchers.

Somehow it's tough to sympathize. After all, it's not as though these executives are actually listening to their critics. They've exhaustively patented the technologies behind the GeneChip, and defended them aggressively with lawsuits, all in the name of owning the microarray market. What's more, the company has been amply rewarded for its bully tactics on Wall Street. Despite having generated only $96.9 million in revenues last year - and never having turned a profit - Affymetrix has seen its stock climb as much as 700 percent in 12 months.

Besides, I assert, Affy's situation isn't comparable to securing leadership in routers or semiconductors. This is an ethically contentious arena. What we're talking about are, ostensibly, the keys to the mysteries of all life on this planet. At the very least, the DNA microarray - a testing platform that will allow scientists to examine how genes in plants, animals, and humans are affected by just about any chemical or compound - should prove to be the most valuable biological research tool since the invention of the microscope. The small glass chips, printed with

DNA material representing thousands of genes, can be subjected to every potential new drug, every component of food - anything that affects how genes work. This could change the very nature of scientific research. In short, I remind them, there's a lot at stake here.

Over the next month, this group of executives will have good reason to feel picked on. Six days from now, in the wake of a breakdown in talks intended to hasten cooperation between the publicly funded Human Genome Project - the effort to map every gene in the human body - and the private effort of a company called Celera to do likewise, President Clinton and British prime minister Tony Blair will declare that genetic information - the blueprint of life - belongs to everybody.

Their mid-March pronouncement will receive global media coverage, incite a rancorous debate about whether human genes can be proprietary corporate information, and decimate the market value of any company hoarding such data (sending Nasdaq's Biotech Index into a 300-point freefall well before the rest of Nasdaq followed suit). While Affy doesn't generally patent genes - but rather, the tools that enable gene research - the company will be taken along for the ride. Then, three weeks later, Affymetrix will lose part of an important lawsuit filed in a UK court by a renowned British scientist using a page out of Affy's own litigious playbook - a judgment that could spell real trouble for the company. Affymetrix execs will swear they'll appeal. But still, these two events will send the firm's market cap tumbling. While researching this story, I will watch Wall Street rip more than 70 percent out of the company's valuation - from $8.1 billion to $2.4 billion.

From an investor's perspective, it's been a tough first quarter. And such swings are precisely what make biotech a dangerous, and exhilarating, vehicle for businesses and investors alike. It's a chaotic place - equal parts promise and risk - subject not only to cutthroat competition but to a wild-card factor, as well: emotionally charged public attention. Add in the arcane nature of the business, which means, frankly, that most investors don't know what they're buying, and the smallest piece of news can send everyone scurrying. On one hand, then, Affy's fate depends on the same classic challenge as Cisco's: execution of a market-control strategy. On the other, not at all. Biotech isn't information technology.

The assembled officials know all this, of course. Every soon-to-be-public biotech company makes these arguments in the risk-assessment portion of their SEC filings. But today, the Affymetrix chorus unanimously disagrees with the suggestion that biotech is different. Business is business, they say, and in a booming microarray market, it takes aggression to seize opportunity. The company came to the marketplace first and shored up its patents. These executives did everything right, and the microarray now belongs to Affymetrix. Period. "People are assuming this is going to open up," executive vice president Nussbacher says of the array business. "We are fighting very hard to keep that from happening. We don't think it should."

In other words, Nussbacher is suggesting that anybody hoping to come into the array business (for now, Affy is the only company shipping product in any real volume) had better pay homage, and a lot of licensing money, to Affymetrix - or continue to face lawyers swinging Louisville Sluggers issued by the US Patent and Trademark Office. What Nussbacher doesn't realize is that his swagger scares people - it's the type of attitude that attracts the negative attention this group is complaining about.

But in the days before the carnage on Wall Street and in the courtroom, Affy's CEO may be getting the message. Fodor knows we're talking about a delicate subject: a technology that could lead to scent triggers tempting you buy perfume at $135 per ounce, corn that prevents osteoporosis, or even a cure for breast cancer - and this kind of stuff touches a public nerve. Affymetrix has to be cautious, especially in the presence of a reporter. Fodor cautions Nussbacher: "We have to be careful not to project that image."

Behind the Zipper

To understand the GeneChip and the business around it, you need to understand a bit about microarrays in general. To get there, you have to know a little bit about DNA. Start by looking at your zipper. Think of it as the DNA double helix. Now unzip it. One side of the zipper - including one tooth, and the fabric that holds that tooth in place - is the rough equivalent of a basic unit of DNA, known as a nucleotide. The tooth is one of the four chemical bases that make up DNA: guanine (G), adenine (A), thymine (T), and cytosine (C).

Each tooth wants to mate with a tooth on the other side of the zipper, but these bases are picky: T will stick to A, and G will stick to C. When a base from one side finds its mate on the other side, they form a base pair and (OK,

zip up - slowly) the DNA double helix is re-formed.

The union of enough of these base pairs constitutes a gene. Variations in the arrangement of the pairs will create different genes. In all, about 3 billion base pairs make up the estimated total of 100,000 human genes.

The 100,000 human genes contain about 3 billion base pairs. Previously forced to sort through those pairs one or two at a time, researchers can now use microarrays for mass testing.

Differences in base pairs make some people tall, or blond, or prone to tumors. Abnormal changes in these base pairs, called single nucleotide polymorphisms, or SNPs, might be the root causes of most noninfectious human diseases, including cancer, diabetes, and cystic fibrosis. Right now, nobody knows how many SNPs exist, but arrays will help geneticists zero in on them.

A microarray - also known as the biochip, the DNA chip, and a host of other trademarked names belonging to Affy competitors - is actually a simple, passive device. It's merely a tiny glass square onto which the company places one side of the unzipped nucleotides in a known position. These nucleotide "probes" are then washed with a test sample of an unzipped and specially marked strand of DNA derived from, say, a cancer patient's blood.

The unzipped nucleotides in the sample will find mates with unzipped probes on the chip. If a scientist is looking at, for example, a cancer-related gene on Affymetrix's P53 array, he will observe how bases from cancer DNA differ from mates with the probe DNA. Through this process (called hybridization, a version of which was patented in 1987 by a Yugoslavian scientist named Radoje Drmanac), scientists can literally see how normal nucleotides turn into cancer causers.

Like almost everything else about them, even the origins of microarrays are contested. Most agree that Oxford University professor Edwin Southern, the originator of the Southern Blot, an early DNA sequencing technique, was the first to come up with the principles behind the microarray. He applied for patents on his concepts in the UK in 1988. Those patents are now well-known, and are widely referred to as the Southern Patents.

The years that followed brought several different manufacturing methods from various teams of researchers. In 1991, a team led by Fodor, who was at the time working at the Affymax Research Institute in Palo Alto, California, published a paper in *Science* describing the creation of a microarray based on the same photolithographic technology used in the manufacture of computer microchips. Later, a team at Stanford University developed a new method - an early version of the spotted array technique - by depositing minuscule spots of DNA onto a glass slide via a method similar to offset printing, with the DNA material serving as the ink. A few companies, like Caliper, are now making arrays using microfluidics, running the chemistry through channels a few microns wide.

Deep Impact

To get an idea of how important the microarray is, consider the Human Genome Project. When project researchers finish their work sometime in the next couple years (the rival effort by the Celera unit of PE Corporation announced in early April that it had completed the mapping of the genome of a human being), they will have realized the approximate location of the genes and found most of the letters that make up those genes. But that's a far cry from knowing the precise order of the letters - much less what the letters, in conjunction, really say.

In effect, researchers will have pulled up to an empty library and dropped a load of billions of As, Cs, Gs, and Ts in a chaotic heap. Until the microarray, scientists trying to make sense of the letters would have had to pick through that heap a few nucleotides a time. Now they can work on a mass scale: For the first time, researchers have a printing press onto which they can load their letters and publish complete books.

The financial implications of this development are obvious to everybody in gene research. Already, pharmaceutical companies - eager to cut the long odds (about 10 to 1) of successfully bringing a drug to market - have begun gobbling up all the genetic data they can find so that their drugs can be tailored more precisely. Some of the companies rocketing the Nasdaq to new heights earlier this year - Celera, Incyte, Hyseq, Human Genome Sciences - have been catering to that new hunger by building huge data banks of proprietary letter

sequences, then selling access to that information.

Typically, if a drug company finds a sequence useful in the creation of a drug, genomics firms will receive royalties for the use of their patented data. This "reach-through" payment scheme - the ability to make money at both the front and back ends of drug development without exposure to the vagaries of drug testing and approval - is one reason why shares of these genomics companies soared in the first place. It also explains why investors panicked at the slightest hint of possibility that the rights of genomics companies to patent gene sequences could be questioned.

But, unlike genomics companies, Affymetrix doesn't usually patent sequences; it simply provides a testing platform for sequences. With a GeneChip, scientists can test a given compound on many sequences at once. They can see the results in hours - instead of days or months - and use those results to pinpoint promising compounds for further development, or to steer clear of dead ends.

The payoff for array makers could be huge, thanks to the research money that's chasing good tools. Pharmacia & Upjohn alone spent about $1.4 billion on R&D in 1999. Multiply that by what's spent by every other large drug maker, every agribusiness looking to make a new breed of superfood, and every corporation frantically searching for the genetic basis of everything from chocolate cravings to what makes roses smell the way they do, and the market for biochips seems limitless.

Amazingly, these applications might be just the beginning. The big payoff, say microarray experts, will be in analyzing single nucleotide polymorphisms and the rogue disease-causing proteins those SNPs create. SNP analysis will usher in the day of pharmacogenomics - custom drugs that treat each person's mutations. And in about a decade, experts maintain, physicians - and even parents with children home sick from school - will possess handheld microarray devices capable of revealing whether Susie's sore throat is a strep infection, and if so, which strain. Today, that very process involves taking a throat culture and waiting days for lab results.

According to several executives at companies hoping to compete for the microarray market, this has the potential to be a $10 billion-a-year industry within a decade. To put that in perspective, that's more than five times the total annual sales of Epogen, Amgen's blockbuster bioengineered treatment for anemia. In short, Affymetrix is in the fortunate position of selling most of the hammers to the construction companies at a time when there's a whole lotta building going on.

The financial implications of microarrays are obvious - and huge - to anyone in gene research. Biochips promise to become a $10 billion-a-year industry within a decade.

Bio-Bubbles

And Affymetrix has already sold a lot of hammers. The company's shipment of some 100,000 GeneChips in 1999 reflects its position as the only microarray company to fully commercialize its product for a hungry marketplace - while would-be competitors are still in the beta-testing phase. Affy's revenues nearly doubled in 1999. Net losses - attributable to research and development as well as to costs associated with ramping up mass production - dropped to $1.02 a share last year, from $1.11 a share in 1998. CFO Hurwitz says he's expecting Affy's first profit in the fiscal fourth quarter of this year.

Do numbers like these justify that 700 percent run-up in Affy stock? Hardly. But there's a feeling that the GeneChip system has already become pervasive within both the pharmaceutical industry and academia. ("Everyone has an Affy," says Eric Neumann,vice president of life science informatics for Third Millennium, a Cambridge, Massachusetts-based consulting firm.) Which is more than enough for money-gorged Net-stock investors who - done with ecommerce plays - have set off in search of the next big thing. The Affymetrix situation has, in turn, inspired an onslaught of initial and secondary public offerings from competitors, thus creating a good old-fashioned Wall Street feeding frenzy for the stocks of any company even close to Affy's space.

Of course money managers have seen all this before. Ten years ago, a biotech stock bubble sent valuations soaring. Back then, investors didn't realize how much time and money are spent between research and actual development. Sure, there were a couple high-profile successes, like synthetic human growth hormone, but the returns couldn't justify the big financing - and the burst was so pronounced that investors stayed away from the

industry for the better part of a decade. "I was in the middle of all that," says Rick Johnston, the man who runs Incyte's microarray research and manufacturing facility in Fremont, California. "There was an interest in biotech because it held all this promise. But ultimately, it left a sour taste in the mouths of investors."

This time it's different, Johnston argues. In fact, he says, today's excitement is about the fulfillment of those decade-old hopes. That is, it has simply taken this long to effectively use the innovations of those early days. Techniques like automated gene sequencing, polymerase chain reaction (which makes many copies of sequences), and sequencing via hybridization are now foundation technologies that enable the new genomics revolution - and they all contribute to the technology of microarrays, the tool that may make this revolution real.

Rocky Beginning

While Affymetrix is in a prime position to benefit from the renewed interest in biotech, how the company fares may depend on its ability to wade through its current legal morass and cope with pricing and manufacturing woes. The seeds of these troubles were planted when the company was an amorphous Netherlands-based research firm called Affymax, founded in 1988 by Alejandro Zaffaroni, the Uruguayan entrepreneur who brought us the nicotine patch. Affymetrix spun out of Affymax in 1993 on the strength of Fodor's idea to use photolithography manufacturing to cram many nucleotide probes onto a small chip. The idea was brilliant, but it was also a trap.

Photolithography, in effect, plugged Affymetrix into Moore's law by allowing the steady increase in the number and density of nucleotides on each chip, thus reducing the manufacturing cost per probe. But increasing the number of nucleotide probes makes the chips themselves expensive and difficult to manufacture.

The process involves coating each chip with a photoreceptive chemical, laying down thousands of probes, and using 70 separate light masks to selectively activate a probe pattern. Probes not exposed to light remain inactive. Probes hit by light become active and usable for testing. Gaps between the probes measure a mere 100 angstroms - roughly the space occupied by 66 hydrogen molecules - which requires the manufacturing process to be perfect, lest a researcher end up looking at the wrong probe.

Partly due to the potential for mistakes, many of the probes are actually redundancies - checks put in place to ensure the researcher is testing what he thinks he is. Even with these safeguards, says Jonathan Aschoff - an investment analyst with Sturza's Medical Research, a financial analyst firm specializing in medical and biotech companies - up to 50 percent of the chips Affy makes fail the company's own quality control inspection. As recently as last year, another 20 percent of those that actually shipped would still fail upon arrival, according to Affymetrix's biggest customer, Gene Logic.

Coupled with insufficient manufacturing capability, that kind of inefficiency translated to a 70-day order backlog last year. Of course Affy is aware of these problems. Company officials insist quality is improving - the post-QC failure rate is down to the single digits, they say. What's more, now that the Sacramento, California, manufacturing plant is running, chips are sometimes shipped within days of an order.

On the road to maximizing manufacturing efficiency, Affymetrix has also learned a thing or two about pricing. At first, the company mimicked the reach-through method employed by gene data-bank companies - but it became clear that the scheme was not a good fit. "When we started out, we were trying to price the product low so that when we sold the chip, we got a downstream drug royalty," recalls Norviel. "We quickly figured out that wouldn't work."

For one thing, with high up-front costs of its own, Affy couldn't afford to wait for royalties. Besides, big pharmaceutical companies objected to giving Affymetrix a cut of sales. So Affy decided to charge a bundle for its chips - anywhere from $100 to $2,000 each.

Big pharma undoubtedly felt the effects of that restructured pricing plan. Any given experiment will likely require not only several chips but also a machine (in Affy's case a laser scanner) to read the results, and computer equipment and software to interpret data. The package just to get started, according to Affy officials, is generally about $188,000. Tack on the price of several experiments and that number quickly jumps north of $250,000.

Today's applications are just the beginning. Coming up: Handheld arrays that test if a sore

throat is a strep infection, and "pharmacogenomics," personalized disease-treating drugs.

Given those numbers, it's easy to see why the new pricing structure hit the typically resource-starved academic researchers hardest - and they reacted in differing ways. Some offered to share intellectual property rights in return for chip discounts, according to Nussbacher. Others balked, believing such sharing would lead to restrictions on an academic's right to publish results of experiments and to profit from discoveries.

In a statement issued to researchers last June, the University of California made it clear that the Affymetrix supply agreement "impacts ... on your intellectual property rights and your ability to share research results relating to your use of Affymetrix chips or data resulting directly from chip use." In fact, according to the UC statement, "Because of the long period for which Affymetrix has some rights to inventions, you may need to consider the implications to future research sponsors of the potential reach of Affymetrix intellectual property rights."

Fodor emphatically denies the insinuation - that his company has reach-through in the academic community. An academic access agreement addendum Affymetrix supplied to *Wired* mostly supports his assertions, though it does contain several restrictions on the use of GeneChips and data.

Fodor says the company's rights to any researcher's inventions are extremely limited. The terms of the agreement, he argues, are such that if a GeneChip helps a researcher discover new nucleotides, Affymetrix has the right to negotiate a license to include them on its chip-array products. "We did negotiate reach-through with one university and a specific researcher, and it just came back and bit us," Fodor acknowledges. "We dropped the whole thing, but it was a black mark that took a long time to wear off."

Unleash the Lawyers

The resentment that has built up around Affymetrix - for its pricing structure as well as the stalled manufacturing process - tilled the soil for competitors. At first, the challenges bubbled up from scientists who realized they could make their own arrays with the Stanford-style spotting technology. Stanford professor Patrick Brown even established a Web site and discussion group that provided detailed instructions, drawings, and advice on how to do it.

The "roll your own" movement caught on. So much so that Affymetrix acquired Genetic MicroSystems of Woburn, Massachusetts, a manufacturer of array spotting systems, to cater to the growing faction.

Next came competition from Affy clients and partners frustrated by their lack of control. A nasty outbreak of lawsuits erupted, including one that could mean life or death for Affymetrix.

In 1997, Incyte was looking to gather more data for its library and perform experiments for corporate subscribers. The company considered buying Affy's GeneChips, says Johnston, but opted instead to purchase a small chipmaker called Synteni, which had sprung out of the Stanford array effort. Synteni's contact printing technology resulted in dense - and cheaper - arrays. Though Incyte used the chips only internally, Affymetrix sued, claiming Synteni/Incyte was infringing on its chip density patents. The suit argues that dense biochips - regardless of whether they use photolithography - cannot be made without a license from Affymetrix.

Incyte countersued and has since filed suit against genetic database competitor Gene Logic for infringing Incyte's patents on database building. Meanwhile, Hyseq sued Affymetrix, claiming infringement of nucleotide hybridization patents obtained by its chief scientific officer, Radoje Drmanac. Affy, in turn, filed a countersuit, claiming Hyseq infringed the spotted array patents. Hyseq then reached back and found an additional hybridization patent it claimed that Affy had infringed. Hyseq is suing for four patents - all of which involve the nucleotide hybridization patent obtained by Drmanac.

Many in the industry seem to feel that Affy's claims are outlandish. It's as if, they say, upon producing the first Model T, Henry Ford had tried to gain the rights to the very idea of the automobile, and obstructed anyone who tried to develop anything with four wheels. "Affymetrix is certainly trying to leverage a proprietary position," says Paul Boni, who until recently was an analyst with Punk, Zeigel & Company. Incyte general counsel Lee Bendekgey says the suits are a matter of "whether what they invented covers all kinds of microarrays or whether it just involves a particular type of microarray manufactured using a particular process."

Norviel will have none of the obstruction argument. "That's what people who don't want to pay say," he counters, insisting that Affymetrix has an aggressive licensing policy that allows others to enter the market. "We have a standard licensing program. It's a two-page form. Most people rumple the pages a little bit, roll their eyes, and say, 'Oh, you are so expensive,' and then they sign. You don't get any of this foolishness."

To further its goal of becoming the standard array, Affymetrix has also tried to standardize the all-important data-handling steps involved in interpreting array test results. In late 1997, Affy joined with Molecular Dynamics to form the Genetic Analysis Technology Consortium (GATC), a software standard designed to favor Affy hardware. Affymetrix now advertises its technology as GATC compliant, and, in an obvious effort to make GATC - and therefore the GeneChip - the standard, Affy's academic access agreement requires scientists to "make reasonable efforts to transfer data ... in accordance with the GATC standards group whenever possible." Not surprisingly, this move has ruffled feathers, too.

"GATC is not the most modern, up-to-date scheme," explains consultant Eric Neumann, noting that a new program called the Microarray Gene Expression Data Base is being developed in response to GATC so that results from multiple microarray technologies can be cross-analyzed. "It frees you from one vendor, and it's an open consortium ... Affymetrix can't have complete control of all the pieces. Nobody can."

It's this sort of controlling move that has led some in the industry to relish Affy's most recent - and most potentially damaging - legal battle, the fight with Edwin Southern. The firm Southern founded, Oxford Gene Technologies (OGT), filed suit against Affymetrix in June of last year, accusing the company of infringing the Southern Patents and attempting to obtain a license illegitimately. "Every array they make infringes the patent," says Chris Shelley, Southern's UK solicitor.

With an April 7 UK verdict coming down in favor of Southern, Affymetrix is on the spot. Yet its chances are good, Fodor says, because Affy's patents are ironclad and Southern's weak. Still, Affy was concerned enough about the Southern Patents back in 1998 to enter into negotiations with OGT to obtain access to them. In June of that year, Affy was about to agree to pay $20 million and grant OGT a cross-license in return for access to the Southern Patents. But fearful of letting OGT have access to its patents, Affy called off the negotiations in August.

> **Affy's market share, tight control, and pricing structure have built up strong resentment, and tilled the soil for competitors ranging from upstarts with new tech to manufacturing giants.**

Instead, the company made a deal - Shelley called it a "ruse," and Justice Robin Jacob, the presiding judge in London, agrees - with Beckman Coulter, an instrument maker then licensed under the patents. Affy agreed to enter into a consortium with Beckman Coulter, or, if OGT refused to give the "consortium" a license, to buy Beckman Coulter's embryonic array business for $5.9 million and throw in another $5 million of research work. In other words, Affymetrix would get access to the Southern Patents for almost half price.

Nussbacher explains the paradox of denigrating Southern's patents even while going through contortions to get at them: "There's a lot at stake with the market cap we have, and if you can mitigate that risk with a couple million dollars, we'll do it, sure."

The machinations may cost Affy more than "a couple million dollars." Affymetrix put up a fight over the Beckman Coulter deal because it said the license it obtained precluded any infringement of Southern's array patents. But the UK judge struck down the deal, so now Affy will have to prove - in the UK and in the US, where the case comes up in October - that it's not infringing. Even Fodor admits that this could be a problem. "It's not clear yet what the patent office is going to grant Southern. There's still a question whether or not the patents he's going to get will cover us."

Those familiar with the world of microarrays say the Southern Patents can't be brushed off. In fact, in December of last year, first Incyte and then Agilent obtained array licenses from Southern. "If we didn't think they were valid patents, we wouldn't have bought them," says Incyte's Lee Bendekgey.

Justice Jacob offered a solution in his summary. "In principle OGT [was once] willing to grant a license to Affymetrix. Indeed, they probably still are. Notwithstanding the fact that they have started infringement proceedings, there may be a negotiated outcome, including a license."

So Affymetrix may find itself in a cross-licensing deal after all. Indeed, it may have no choice. If it refuses and loses on appeal, Southern's solicitor Shelley says, "OGT can close [Affymetrix] down."

Big Competition

While a shutdown at the hands of OGT seems unlikely, Affymetrix still could be headed for a rough patch. Many say the biochip segment is taking the path of microprocessors, with a tumultuous legal beginning followed by licensing and niche marketing. But Affymetrix is trying to throw a wrench into the works. "Semiconductors were in this position for 10 or 15 years, and that got sorted out," Hyseq president and CEO Lewis Gruber says of the mess. "It's not that we're behind the curve in rationalizing markets and cross-licensing. But you have a strong resistance on the part of Affymetrix to doing anything of that sort. They have relied on telling people they are - and will be - the only chip on the market."

This posture has done nothing to put more arrays into the hands of the people clamoring for them (Harvard professor George Church says it has been "pathological to research"), a fact that has spurred even more competition. "The people who need to use the stuff, both pharmas and the academic community, don't like infighting," Neumann explains. "They want to see results."

So companies like 3M, Agilent, Motorola, Corning, and Hitachi - none of whom are intimidated by Affy's patent portfolio - as well as a host of small players are lining up to break Affymetrix's hold on the market. Every new entry has formed one or more alliances with pharmaceutical and equipment companies who are themselves often signed up with several different array makers. "This is just unbelievably dynamic," says Incyte's Johnston. "It's tough to know who to bet on. I don't think you can bet on any one technology. If you look at big pharma, they're at the roulette table, just putting bets everywhere."

PE Corporation illustrates that point. PE, parent company to Celera, has acquired Third Wave, an SNP detection company based in Madison, Wisconsin; it also provides mass spectrometry equipment to another SNP analysis firm, Sequenom, of San Diego; and it collaborates with Hyseq. PE is also working with 3M to develop 3M's array and has put up $5 million to finance Illumina, a San Diego array company.

Affy is also at risk from smaller upstarts. Illumina is using licenses from Tufts University to mount micron-scale beads with attached nucleotides into the tips of optical fibers. And it employs Mark Chee, an array inventor who worked with Fodor at Affy. Lynx, based in Hayward, California, is using beads that, according to company president and CEO Norrie Russell, can do gene-expression analysis on all 20,000 to 30,000 genes that a cell expresses. Financial analysts think the Lynx system, which BASF and DuPont are testing, could be a powerful competitor. The National Institutes of Health makes its own arrays - 5,000 last year - using print-spotting, and it's trying to develop new technologies to place in the public domain or license to the highest bidder.

But the biggest threat is coming from the industrial-scale manufacturers. Corning and Motorola plan to unveil platforms sometime this year. Nick Naclerio, formerly with Darpa and now VP and general manager of Motorola's new Biochip Systems, says Motorola will market high-density array technology that grew out of collaboration with Argonne National Laboratory. "We're developing arrays like Affy's or Incyte's or Hyseq's," he says, "but also microfluidic chips like Caliper's and new detection technologies." He says the chips work with an electronic detection process and that Motorola "can guarantee the quality of the probes going on the chip. Affy can't do that. We can."

It's the recently spun-off division of Hewlett-Packard known as Agilent, though, that's gone from being Affy's partner to its archenemy. In 1994, Affymetrix and HP struck a deal for HP to create an Affy-compatible confocal laser scanner to illuminate the fluorescently labeled nucleotides. Under the terms of the agreement, any customer who buys a complete system before 2003 gets a bundled HP/Affymetrix GeneArray scanner. But last winter Agilent announced it was going after the microarray business, a move that sent Affy executives back-pedaling on their partner's prowess. "HP has a big market in communications and all this other stuff," Fodor says. "How serious are they?"

Fact is, Agilent is further along the path to marketing a product than any of the other big players. To add insult to injury, it has linked with another former Affy customer, Rosetta Inpharmatics - a Seattle-area microarray firm that grew out of labs at the University of Washington - to create a high-density, inkjet-spotted array. Now Affymetrix finds itself in the awkward position of selling a competitor's scanners until 2003. "I guess we didn't

expect this sort of behavior out of HP," Fodor says glumly.

HP spinoff Agilent may prove to be the biggest threat to the GeneChip's dominance. But users want arrays now, amid the rising genome data flood. The first mover has the advantage.

"They worked with us, and now they covet the space," Nussbacher adds, accusing Agilent of using Southern as a front to attack Affymetrix.

Knocking Affy off the Throne

No matter who gains footholds, the price of arrays is about to drop - a lot. Which is why Incyte president Randy Scott says he's "enjoying the entrance of Motorola, Agilent, and Corning." Neumann and Incyte's Johnson think microarrays will even soon be priced as "a commodity item."

Affy executives realize that prices will fall, but downplay the effect that will have on their business. "Our costs should drop at least as fast as our prices," CEO Edward Hurwitz says. "Our margins will be sustained or improved over time."

Affymetrix also has an impressive balance sheet, including $225 million in cash reserves as of December 31 and still-sizable valuation, to buy its way out of an onslaught. Most likely, the company will drop Agilent when the scanner deal expires and make use of recently acquired instrument company Genetic MicroSystems.

Threats from innovations will be absorbed, too. "We're becoming a full-fledged operating company, and the way leading-edge companies stay that way is to go out and acquire and partner with technologies they can't invent," Hurwitz says. "Sit tight for the next 6 to 12 months and you'll see us make outright acquisitions and invest in the next generation of companies."

The only problem is that the big boys will shop, too. Which means Affymetrix could find itself in a bidding war against companies with annual revenues in the billions of dollars.

Ultimately, when it emerges from the battles of the next year or so, Affymetrix is likely to have fallen from its place as the Kleenex or Q-Tip of the array business. But that doesn't mean Affy is going away. As with most distracting corporate legal skirmishes, odds are that Affymetrix and Incyte will settle. The Hyseq stew appears to be on low boil, and while the Southern suit is a danger - even in what's likely to be a more conservative, Affy-friendly US court come October - the matter seems destined to result in some kind of cross-licensing arrangement.

Meanwhile, saying you can make arrays is one thing, but making them is another. Thus far, only Affymetrix has made microarrays in any volume for outside customers. In genomics, as in comedy, timing is everything. Users want arrays now, while the data flood from genome research spews. Many customers won't want to wait until the bugs are worked out of competing technologies.

Also, Affy's GeneChips win good reviews for the density of their probes and for the readability of their data, making them especially valuable for the niche that calls for big-picture looks at how genes turn on or off. Finally, Affymetrix is a known quantity, and some heavy investments have already been made by users reluctant to switch. The first mover has the advantage.

Just don't expect clear answers about winners and losers anytime soon. "It's all pretty nutty," laughs Robert Cohen, a consultant with Front Line Strategic Management, a Bay Area firm. "The genomics sector is driving a lot of the nuttiness. There are so many options, so many components and parts-making systems. It's all a bit dizzying."

"It will get worse before it gets better," agrees analyst Aschoff.

Meanwhile, the tension between commerce and the ethics of access to biotechnology miracles will continue to rise. "My personal view is that this field needs to be opened up," Edwin Southern says. "There are important and

deep issues here that shouldn't be directed by narrow commercial concerns."

Of course Affymetrix cares about human betterment, company president Siegel says. But "it's not fair to our shareholders to just give up the technology. Everyone would love a piece of this pie - love to compete free and clear. Affymetrix has done a tremendous job of building up the patent estate, so we are an incredible target. People love to pick on us. We are viewed as an evil empire."

Indeed, if its business was IT, Affy would be revered. But at the end of the day, it's not - and that's something Affymetrix has yet to come to terms with.

Brian Alexander (alxander@pacbell.net) *wrote about life extension in* Wired *8.01.*

EXHIBIT 11

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 12

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